Strategic Functionalization of Indoles and Oxidative Coupling Reactions

A thesis submitted in partial fulfillment of the
requirements for award of the degree of

Doctor of Philosophy

Dipika Konwar

Registration No. TZ201063 of 2019

School of Sciences
Department of Chemical Sciences
Tezpur University
Napaam-784028, Tezpur
Assam, India

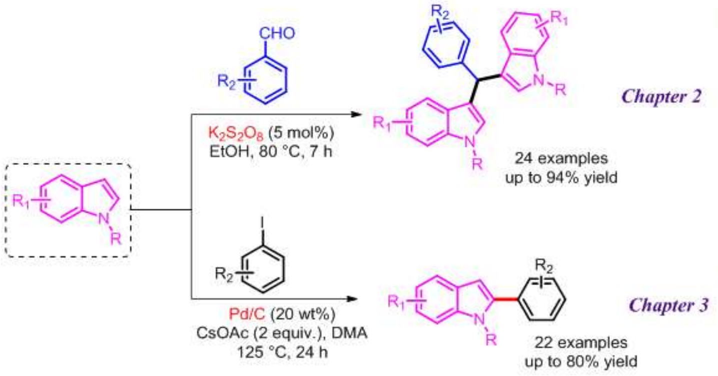
March, 2023

Chapter 7

Conclusion and Future Scope

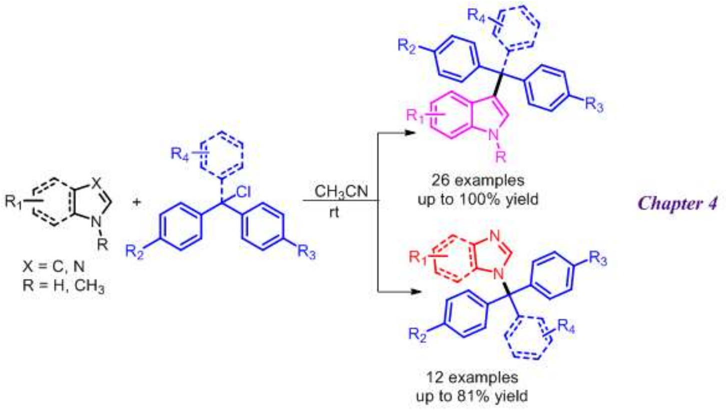
7.1 General Conclusion

Functionalization of indole at C-2 and C-3 positions and oxidative coupling to form C-C bond are mainly focused in the thesis. The first three work chapters (Chapters 2, 3, and 4) are comprised of indole-based functionalization reactions. The remaining two chapters (Chapters 5 and 6) describe the oxidative coupling reactions. The schematic representation of the experimental chapters is shown below:

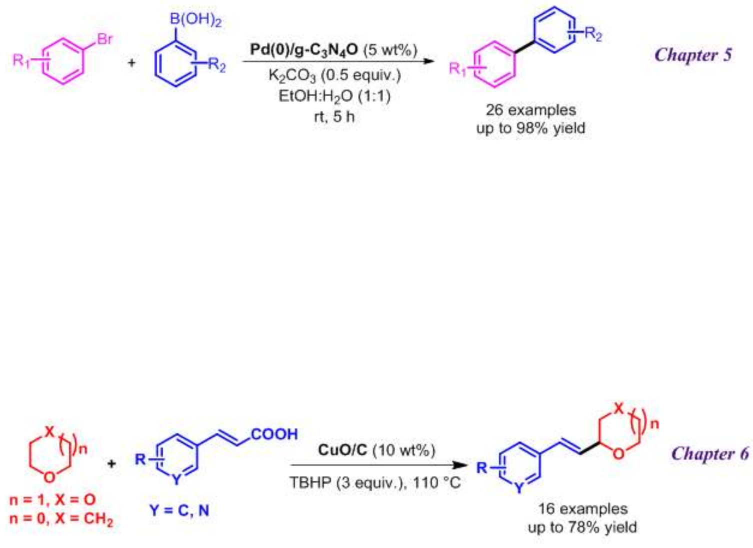


Free radical triggered convenient synthesis of bis(indolyl)methane using various indole and aldehyde derivatives with potassium peroxodisulfate as catalyst under the ambient conditions is developed.

C-2 selective direct functionalization of *N*-methylindole derivatives with aryl iodides catalyzed by Pd supported on carbon is developed without using any ligand or directing group.



Halogen bonding assisted selective C-3 and *N*-benzylation of nitrogen-containing heterocycles using trityl chlorides is investigated experimentally under catalyst-free conditions at room temperature in acetonitrile.



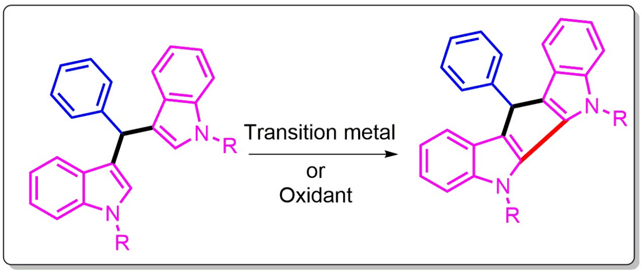
Pd nanoparticles supported on a graphitic carbon nitride oxide (g-C_3N_4O) sheet is developed as an efficient heterogeneous catalyst for Suzuki-Miyaura cross-coupling reaction under limiting basic conditions. The developed bio-catalyst, Pd(0)/g-C_3N_4O provides excellent yields of the desired cross-coupled product just under a sub-stoichiometric amount of exogenous base.

Direct C-H bond functionalization of cyclic ethers through decarboxylation by using electronically diverse cinnamic acid derivatives in presence of synthesized biogenic CuO/C nano catalyst is developed.

Figure **7.1**. Schematic representation of experimental work

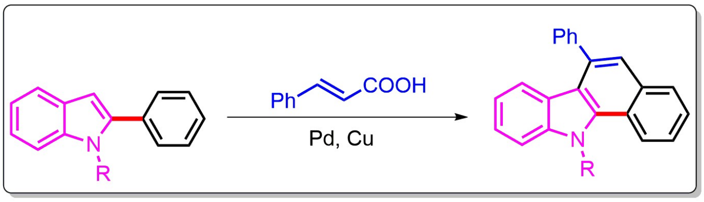
7.2 Future Scope

The present work discussed in the thesis can be extended further to carry out different useful transformations. Bis(indolyl)methanes can be further used for the synthesis of carbazole type compounds in presence of transition metals or oxidants (Scheme **7.1**).



Scheme **7.1**. Carbazole type compound from BIMs

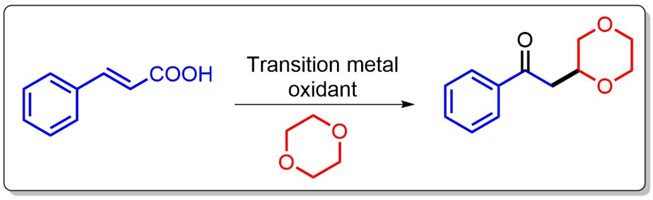
To obtain C-2 selective functionalized indoles in absence of any ligand or directing groups, we should try to develop modified Pd catalysts to carry out the selective functionalization under mild conditions. This C-2 functionalized product may undergo annulation type reaction with cinnamic acid catalyzed by transition metals (Scheme **7.2**).



Scheme **7.2**. Annulation type reaction of C-2 arylated indoles

Similarly, we should explore new polyaryl group containing benzylating sources for C-3 and *N*-benzylation of nitrogen-rich heterocycles. By studying the behaviour of different solvents we should try to find out solvents that trigger the halogen bonding.

The C-C bond formation through Suzuki-Miyaura cross-coupling can be further modified with a new base functionalized Pd catalyst in order to carry out the reaction either in catalytic amount of base or base-free conditions. For decarboxylative alkenylation of cyclic ethers with cinnamic acids, except Cu, other transition metal catalysts both in homogeneous or heterogeneous conditions can be employed. We can also synthesize compounds having carbonyl group through decarboxylative coupling of cinnamic acids with cyclic ethers (Scheme **7.3**).



Scheme **7.3**. Decarboxylative coupling of cinnamic acid with cyclic ether